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(54) Title: MUTATIONS OF VOLTAGE-GATED ION CHANNELS THAT ALLOW THEM TO EXPRESS A VOLTAGE-INDEPENDENT PHENOTYPE AND AN IMPROVED METHOD TO USE THE SAME

Alignment of Voltage-Gated Potassium Channels Relevant Regions

hKv1.1	PYFITIATEIAEQEGNQKGEQATSLATLEVTRIVEVTRIFET,SRHSKG
mKv1.2	PYFITLGTELAEKPEDAQQGQQAMSLAILMYIRLVRVFRI FKLSRHSKG
Kv1.4	PYFITIGTDLAQQQG ·- ·· GGNGQQQQAMSFAILRIIRLVRVFRIFKLSRHSKG
Kv1.3	PYFITLGTELAERQGNGQQAMSLAILRVIRLVRVFRCFKLSRHSKG
hKvl.5	PYFITLCTELAECOPCC GGGGQNGQQAMSLAILEVIELVRVFRIFKLSRHSKG
ShakerB	PYFITLATVVAEEEDTLNLPKAFVSPCDKSSNQAMSLAILAVIRLVRVFRIFKLSRHSKG
rKy3.1	PFYLEVCLSCLSSKAVKDVLCFLRVVRFVRILRIFKLTRHFVC
rKv2.1	PYYVTIFLTESHKSVLQEQNVRRVVQTFRIMRILRILKLARHSTG
hKv4.2	PYYIGLVMTDNEDVSGAFV: RVFRVFRIFAFSRHSQC
hKvl.1	LGILCOTLKASMRELGLLIFFIFIGVINTSSAVYFAFAR FARSHFRSIPDA
mKvl.2	LCILCOTLKASMRELGLLIFFLFIGVILF3SAVYFALADERDSCFPSIPDA
Kv1.4	LOILGHTLRASMRELGLLIFFLFIGVILF9SAVYFAEAD ETTHFQ917DA
Ev1.3	LQIIGQTT.KASNRET.GT.LTFFLFTGVILFSSAVYFAEADDPTSGFSSIPDA
hKvl.5	LQILGKTLQASMRELGLLIFFLFICVILFSSAVYFAEADNCCTHFSSIFDA
3haketB	IQILGRIT.KASHRELGILLIFFLFTGVVLFSSAVYFAEAGSENSFFKSIPDA
rKv3.1	LRVLGHTLRASTNEFLLL11FLALG/L1FATM1YYALRIGAQPNDPSASEHTHPKN1P1G
rKv2.1	LQSLCFTLRRSYNELGLLILFI.AMGIMI FEGI.VPFAEKDEDDTKFRS1 PAS
hKv4.2	LRILGYTLKSCASELGFLLFSLTMAIIIFATVMFYAEKGSSASKFTS1PAA
hKv1.ì	PWWAVVSMTTVGYGDMYPVTIGGRIVGSLCAIAGVLTIALPVPVIVSNFNYFYHRETEGE
mXv1.2	FWWAVVSMTTVGYGDMVPTTIGGKIVGS:CATAGVLTIALP/PVTVSNFNYFYHRETEGE
KV1.4	FAVIAVVTMTTVGYGDMXPITVGGKIVGSLCAIAGVLIIALPVPVIVSNTHYFYHRETENE
Kv1.3	PANAVVTMTTVGYGDMHPVT1GCK1VGSLCA1AGVLT1ALPVPVIVSNTHYFYHRETFER
hKv1.5	PWWAVVTMTTVGYGPMRPTTVGGRIVGSLCALAGVLTIALPVPVIVSNEHYPYHRETDHE
ShakerB	PANAVVTNTTVGYGENTPVGVNGKLVGSLCALACVLTLALPVPVIVSNFNYFYHRETDQE
±Kv3.i	EWWAVVTMTTLGYGDMYPCTMSGMLVRAI CALAGVI.TTAMPVPVTVNNFGMYYSLAMAKQ
zKv2.1	FWWATITMTTVGYGDIYPKTLLGKIVGGLCUIAGVLVLALPIPIIVNNESEFYKEQKRQB
hKv4.2	FWYTIVTHTLCYGEN/PKTIAGKIFGJICSLSGVLVIALP/PVIVSNPSRIYHQNQRAD

(57) Abstract: The subject invention includes mutant voltage-gated ion channels that are open over a wide range of potential differences across membranes. The present invention also includes methods of use of such mutant voltage-gated ion channels in cells with highly negative potential differences across their membranes. One preferred mutant voltage-gated ion channel is a channel with a mutation at the residue homologous to P513 in Kv1.5 and at least one mutation at one of the residues homologous to R400, R403, and R409 in Kv1.5.